

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

**INVESTIGATIONAL DEVICE USAGE
IN RESEARCH & DEVELOPMENT SERVICE**

1. **PURPOSE:** To establish a service level policy for the use of investigational devices, including the emergency use of devices at the Portland VA Medical Center.
2. **POLICY:** The Department of Veterans Affairs clinical investigations of medical devices are subject to the Federal Food, Drug, and Cosmetic Act and unless exempted under certain specified conditions, are required to comply with Investigational Device Exemption (IDE) regulations as outlined in 21CFR812. VA investigators are expected to fulfill all of the responsibilities delineated in the Food & Drug Administration (FDA) regulations. Investigational devices in use at the Portland VA Medical Center (PVAMC) must be stored, secured, and dispensed in accordance with specific device requirements and as outlined in the research project. Principal Investigators are responsible for the appropriate storage, security, dispensing, and use of investigational devices at the PVAMC. The investigational devices may only be used at the PVAMC after:
 - a. The research project and associated documentation have been approved by the Institutional Review Board (IRB) and the Research & Development Committee (R&D), excluding exceptions for the emergency use of an unapproved medical device as outlined in this policy.
 - b. The patient or legal representative has signed the VA Research Consent Form (VA Form 10-1086), excluding exceptions from informed consent as outlined in this policy.
3. **DEFINITIONS:**
 - a. An **Investigational Medical Device** is defined as a device, including a transitional device, that is the object of an investigation [21CFR812.3(g)].
 - b. An **Unapproved Medical Device** is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for pre-market approval under section 515 of the Federal Food, Drug, and Cosmetic (FD&C) Act [21 U.S.C. 360 (e)]. An unapproved device may be used in human subjects only if approved for clinical testing under an approved application for an Investigational Device Exemption (IDE) under section 520 (g) if the Act [21 U.S.C. 360(j)(g)] and 21 CFR part 812. Medical devices that have not received marketing clearance under section 510(k) of the FD&C Act are also considered unapproved devices.
 - c. An **Investigation** is defined as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device [21CFR812.3(h)].
 - d. An **Investigator** is an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.
 - e. A **Sponsor** is a person who initiates, but who does not actually conduct the investigation, that is, the investigational device is administered, dispensed, or used under the immediate direction of another individual. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.
 - f. A **Sponsor-investigator** is an individual who both initiates and actually conducts, alone or with others, an investigation that is, under whose immediate direction the investigational device is administered, dispensed, or used. The term does not include any person other than an individual. The obligations of a sponsor-investigator under this part include those of an investigator and those of a sponsor.
 - g. A **Non-significant Risk Device** is one that does not present significant risk to the human subjects.
 - h. A **Significant Risk Device** is one that presents a potential for serious risk to the health, safety or welfare of the human subjects. [21CFR812.3(m)] Such a device is:
 - (1) Intended for use as an implant;

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

- (2) Used in supporting or sustaining human life;
- (3) Intended for a use that is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise preventing impairment of human health; or
- (4) One that otherwise presents a potential for serious risk to the health, safety, or welfare of subjects.

4. RESPONSIBILITIES:

- a. The **Associate Chief of Staff for Research & Development** is responsible for developing and managing policies and procedures related to the use of investigational devices at the Portland VA Medical Center.
- b. The **Research and Development Committee** is responsible for the initial and continuing review of the scientific quality and appropriateness of and approving or disapproving the research projects involving investigational devices with human subjects.
- c. The **Institutional Review Board** is responsible for approving or disapproving research projects involving investigational devices in accordance with the procedures outlined in 5b below.
- d. **Principal Investigators** are responsible for:
 - (1) Submitting the scientific protocol and all required documentation, including the informed consent form and the Portland VA Medical Center Investigational Device Information Record to the Research Service for IRB and R&D Committee review prior to beginning the study.
 - (2) Submitting continuing review documentation and all adverse events to the IRB in a timely manner.
 - (3) Using the investigational device only after notification of IRB and R&D Committee approval and informed consent is obtained.
 - (4) Forwarding the original signed consent forms to the Research Service Office.
 - (5) Adhering to the Investigational Device Exemption regulations at 21CFR812. Research projects involving non-significant risk devices must adhere to the abbreviated requirements at 21CFR812.2 (d).
 - (6) Providing secure storage for all investigational devices according to their storage requirements as defined in the Portland VA Medical Center Investigational Device Information Record.
 - (7) Ensuring that all investigational devices are secured properly as defined in the Portland VA Medical Center Investigational Device Information Record.
 - (8) Providing accountability of all investigational devices as defined in the Portland VA Medical Center Investigational Device Information Record.
 - (9) Maintaining records and tracking of all investigational devices as defined in the Portland VA Medical Center Investigational Device Information Record.
 - (10) Ensuring proper dispensing and utilization of the investigational devices as defined in the research project proposal.

5. PROCEDURES:

a. **Local Research Projects and VA Cooperative Studies**

Principal Investigators must adhere to the following procedures:

A research project proposal must be submitted to and approved by both the Institutional Review Board and Research & Development Committee prior to use of the investigational device. An IDE must be obtained from the sponsor for significant risk devices prior to project review.

- (1) Submit all of the following documentation to the IRB for review:
 - (a) Review of prior data, including risk assessment data previously done by the sponsor and FDA;

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

- (b) Source of the device;
 - (c) Literature survey (this should be a complete substantive review of the peer-reviewed medical literature);
 - (d) Scientific Protocol (protocol design as set forth for devices [21 CFR 812.25]);
 - (e) Initial risk assessment whether it is a significant or non-significant risk device;
 - (f) Portland VA Medical Center Investigational Device Information Record;
 - (g) Significant Risk devices as determined by the FDA or IRB will require the investigator/sponsor to obtain an Investigational Device Exemption (IDE) from the FDA;
 - (h) Expected outcome;
 - (i) Administrative Review Form describing any costs accruing to the medical center;
 - (j) Proposed Informed Consent Form;
 - (k) Initial Review Questionnaire (IRQ); and
 - (l) Any other applicable documentation as outlined in the IRQ.
- (2) Store the investigational device in a locked and secured area as outlined in the Portland VAMC Investigational Device Information Record.
 - (3) Dispense and use of the investigational device is limited to appropriate personnel as outlined in the research protocol.
 - (5) Obtain and document informed consent for each individual prior to using the investigational device.
 - (6) Maintain the appropriate research records and tracking of the investigational device per 21 CFR812.140 .
 - (7) Report the following protocol modifications to the IRB immediately and to the FDA within five days after making the modification. These modifications must not affect:
 - (a) the validity of data or information resulting from the completion of an approved protocol, or the relationship of likely patient risk to benefit relied upon to approve a protocol;
 - (b) the scientific soundness of the investigational plan; and
 - (c) the rights, safety, or welfare of the human subjects involved in the investigation
 - (8) Obtain FDA and IRB approval prior to the following protocol modifications:
 - (a) Device indication;
 - (b) Study control type;
 - (c) Primary endpoint;
 - (d) Protocol modifications designed to terminate a clinical study earlier than originally planned; and/or
 - (e) Increase sample sizes or expand the number of investigational sites.

b. IRB Review of Medical Devices

- (1) The IRB must determine whether an investigational device is either of Significant Risk (SR) or Non-Significant Risk (NSR).
 - (a) The determination of level of risk of the device is based on the proposed use of the device and not on the device alone.
 - (b) The designation of NSR for a device is independent of the designation of a study as minimal risk.
 - (c) The IRB makes its decision of significant or non-significant risk level of the device based on the review and evaluation of the following:
 - ii. the risk evaluation provided by the sponsor or sponsor-investigator;
 - iii. investigator's brochure, if applicable;
 - iv. federal regulations;
 - v. the FDA Information Sheet, "Significant Risk and Non-Significant Risk Medical Device Studies,"
 - vi. any additional correspondence regarding the device that may be from the FDA, sponsor, and/or investigator;
 - vii. the nature of the harm that may result from use of the device;

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

- viii. if the subject must undergo a procedure as part of the investigational study, the IRB must consider the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.; and
 - ix. when applicable, the information and justification given by the sponsor for any NSR determination.
- (d) The IRB may determine a device to be SR even if the sponsor considers the device to be NSR. If the sponsor indicates that the device is NSR, but the IRB determines it to be SR, then the sponsor must obtain an Investigational Device Exemption from the FDA.
- (e) Because NSR studies do not require an IDE, a clinical investigation involving an investigational device classified by the sponsor as NSR may be submitted to an IRB for review without an IDE. The sponsor should provide the IRB with a risk assessment and the rationale used in making its NSR risk determination.
- (f) If the sponsor or FDA has determined a device to be SR, the IRB must also consider the device to be SR during the IRB review.
- (g) The rationale for the IRB's NSR/SR determination must be documented in the IRB minutes.
- (2) The IRB must initially review the risk/benefit ratio of all non-significant and significant risk devices compared to alternative devices and procedures.
- (3) Expedited Review
 - (a) Research projects involving significant risk devices do not qualify for expedited review during the initial review.
 - (b) Research projects involving significant risk devices may be considered for expedited review during the continuing review, if the IRB determines it to be consistent with the research categories published in the Federal Register, Vol. 63, No.216, 11/09/1998: Expedited review of significant risk device studies is allowed at continuing review under certain specified conditions.
- (4) The IRB must determine the frequency of review for research projects involving investigational devices.
- (5) The IRB must review the risk/benefit ratio of the device compared to alternative devices and procedures and approve or disapprove on a continual basis, research projects involving investigational devices.
- (6) The IRB may only approve significant risk device studies only after an IDE approval is obtained by the sponsor. In instances where the sponsor has appropriately obtained a 510(k) or Humanitarian Use Device designation, the IRB may only approve these studies once these approvals have been obtained and verified with the IRB.
- (7) The IRB will notify the investigator and/or sponsor of the review decisions, actions and any needed modifications regarding the research project.
 - (a) If a device study is submitted as SR and the IRB verifies that IDE approval has been obtained by the sponsor, the IRB does not have to notify the sponsor or investigator of the SR determination.
 - (b) If the IRB determines the investigational device to be significant risk and the sponsor has not obtained IDE approval from the FDA, the IRB will notify the sponsor and investigator of its determination.
- (8) The IRB must maintain records for reviewed research project in accordance with the IRB Standard Operating Procedures, which is in accordance with 21CFR56.

c. Emergency Use of Unapproved Medical Devices:

Note: The Food and Drug Administration (FDA) recognizes that emergencies may arise where an unapproved device may offer the only possible life-saving alternative, but an IDE for the device does not exist, or the proposed use is not approved under an existing IDE, or the physician or institution is not approved under the IDE. Using its enforcement discretion, FDA has not objected if a physician

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

chooses to use an unapproved device in an emergency situation, provided that the physician later justifies to the FDA that an emergency actually existed.

A Principal Investigator/Physician must adhere to the following procedures regarding emergency use of unapproved medical devices:

(1) Requirements for emergency use of a medical device:

Note: All three requirements must be met for justification of emergency use.

- (a) A patient is in a life-threatening condition that needs immediate treatment.
- (b) There is no generally acceptable alternative available for treating the patient.
- (c) Sufficient time is not available to obtain prior FDA approval through existing procedures, prior to using the device because of the immediate need.

(2) FDA Physician Expectations Regarding Decision of Use

- (a) Determine whether all three requirements for emergency use have been met.
- (b) Assess the potential benefits from the unapproved use of the device.
- (c) Have substantial reason to believe that benefits will exist.
- (d) Decisions for “emergency” use may not be made in advance of the time of treatment made be needed based solely on the expectation the IDE approval procedures may require more time than is available.
- (e) Exercise reasonable foresight with respect to potential emergencies and to make appropriate arrangements under the IDE procedures far enough in advance to avoid creating a situation in which such arrangements are impracticable.

(3) Notification to the Center for Devices and Radiological Health (CDRH)

- (a) The device developer must notify the Center for Devices and Radiological Health (CDRH) Program Operation Staff immediately after the shipment is made when a device is to be used in an emergency situation meeting all justifiable requirements.
- (b) An unapproved device may not be shipped in anticipation of an emergency.
- (c) Business Hour Contact Information: 301.594.1190.
- (d) Nights and weekends Contact Information: Division of Emergency and Epidemiological Operations: 202.857.8400

(4) FDA Physician Expectations regarding Subject Protection

- (a) Obtain an independent assessment by an uninvolved physician;
- (b) Obtain informed consent from the patient or the patient’s legal representative;
- (c) Notify the PVAMC Chief of Staff;
- (d) Notify the Institutional Review Board; and
- (e) Obtain authorization from the IDE holder, if an approved IDE exists for the device.

(5) After Use Procedures

- (a) Report the use of the unapproved medical device to the IRB within five days of usage and otherwise comply with provisions of the IRB regulations;
- (b) Evaluate the need for the device in the future, and if future use is likely, obtain IRB approval and an approved IDE for future use; and
- (c) If the device does have an IDE, notify the sponsor of the emergency use, or if an IDE does not exist, notify the FDA of the emergency use and provide the FDA with a written summary of the conditions constituting the emergency, subject protection measures, and results.

c. Waiver of Informed Consent Under Compassionate Use or on an Emergency Basis

Note: Even in an emergency situation, the investigator is required to obtain informed consent of the subject or the subject’s legally authorized representative unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23 (a)].

VA MEDICAL CENTER, PORTLAND, OREGON
Human Research Protection Program: Policy & Procedure No. 2

The Principal Investigator/Physician must adhere to the following procedures regarding the exception from informed consent:

(1) Requirements for exception from Informed Consent:

The physician may only waive the requirements of informed consent if all of the following are true:

- (a) The subject is confronted by a life-threatening situation necessitating the use of the test article.
- (b) Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject and there is a medical emergency or urgency.
- (c) Time is not sufficient to obtain consent from the subject's legal representative and there is a medical emergency or urgency.
- (d) No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life and there is a medical emergency or urgency.

(2) After Use Procedures

- (a) Have a physician who is not participating in the clinical investigation, review and evaluate the determination for use in writing.
- (b) Notify the IRB within 5 working days after use of the test article.

6. REFERENCES: 21CFR50

21CFR56

21CFR812

Food and Drug Administration "Guidance for Institutional Review Boards and Clinical Investigators"

Food and Drug Administration "Guidance on IDE Policies and Procedures"

National Committee for Quality Assurance Standards

7. CONCURRENCES: Endorsed by the Research & Development Committee May 19, 2003

8. RESCISSION: HRPP: Policy & Procedure No. 2, Endorsed by the R&D Committee 05/20/2002.

9. FOLLOW-UP RESPONSIBILITY: ACOS Research & Development Service (R&D)

10. REVIEW DATE: May 19, 2006

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